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Pregnancy and Beyond Part IV: Microgravity

SUMMARY

Transport technology in the last 35 years has created new environmental frontiers in which family physicians are, and will continue to be, involved both in research and in administering patient care. Some frontiers address basic physiological problems that cross over into others. In a series of four articles, the author describes six of these frontiers with specific emphasis on pregnancy, from hyperbarism (undersea physiology) to microgravity (space physiology), the problems, and linkages where evident. This fourth article covers the known and postulated effects of microgravity on pregnancy well-being. (*Can Fam Physician* 1988; 34:1461–1467.)

Key words: pregnancy, physiology, environment, microgravity

RÉSUMÉ

Depuis les 35 dernières années, la technologie des transports a repoussé les frontières de l'environnement des médecins de famille qui sont, et continueront d'être, impliqués tant dans le domaine de la recherche que dans celui de la dispensation des soins. Certaines de ces frontières touchent des problèmes physiologiques fondamentaux qui débordent sur d'autres. Dans cette série de quatre articles, l'auteur décrit six de ces frontières en insistant spécifiquement sur la grossesse, de l'hyperbarisme (physiologie sous-marine) à la microgravité (physiologie de l'espace) et leurs problèmes inhérents de même que leurs interrelations. Ce quatrième article explore les effets connus et présumés de la microgravité sur le bien-être du foetus et de la femme enceinte.

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THE YEAR 1987 marked the 30th anniversary of the launching of the world's first satellite. Identifying and solving the problems of man's adaptation to microgravity in space will capture the attention of the scientific community in the 1990s. It is currently projected that in the mid 1990s, the United States, supported by an international co-operative effort, will place in permanent orbit above the earth a 175-ton, 440-foot-long space station costing $39 billion, with six to eight astronauts on board for three to six months at a time.[1] The longest flight to date, within the time frame of planned sojourns on early space-station prototypes, has been that of cosmonaut Yuri Romanenko in 1987, on a Soviet mission lasting 354 days. The moon will likely be colonized by the year 2000, and a Mars mission, which would likely take four to five years to complete, will probably be launched within the subsequent 20 years. The field of telemedicine will burgeon as exploratory space flights and orbits become prolonged. Most of the theoretical concepts of space agriculture on orbiting stations have been worked out to sustain a population of 10 000 people.[2] In the longer future, by the mid 21st century, it is reasonable to assume that there will be flights of 70–80 years duration, into the further reaches of space. The astronauts manning these flights would not be expected to return, and either children launched at flight time or the offspring of the original astronauts would be trained in flight and would be the returning astronauts.[3] A NASA-sponsored conference on space gerontology was held in 1982 to consider these possibilities.[4]

The turn of the century, then, will certainly be an exciting time for microgravity research as we try to understand the physiological penalties and adaptions involved. Canada is currently contributing in two areas: at McGill University on the study of the neurovestibular system and the cause of space motion sickness, and in Vancouver on the study of back pain in space. The problems of space physiology unique to women and, on longer space missions, potentially relating to pregnancy need further study. Although, to date, there have been only six female astronauts of a total of approximately 250, this imbalance will change in time.

Microgravity

There are interesting similarities between the fetal environment and microgravity. One of the physiological models of microgravity is water immersion.[5] However, in contrast to the fetal state, which is one of bone growth in amniotic fluid, prolonged water immersion of the adult produces osteoporosis. Other contrasts between the adult and the fetus for what appears to be a similar state of microgravity are circulatory deconditioning, fluid and electrolyte alterations, muscular atrophy, and anemia.

Osteoporosis

Prolonged space flight produces irreversible bone loss, increased fecal calcium excretion, and toxic renal effects from increased calcium and phosphorus excretion. In-flight animal studies on rhesus monkeys and rodents suggest that the loss is the result of inhibition of new bone formation. In humans, it is not yet clear whether space flight causes reduced bone formation or increased absorption. Autopsies on three Russian cosmonauts who died after 21 days of space flight suggest that the problem may be one of bone resorption.[6] Through long-term microgravity exposure, an astronaut could lose up to 25% of total body calcium in one year of flight.

Studies on the reversibility of bone loss are inconclusive, although as a general rule, an adult human is able to regain only about two-thirds of the calcium lost through disuse. The effectiveness of exercise as a countermeasure is still uncertain, although on long-term Soviet space flights in conditions of weightlessness, calcium loss slowed considerably over three to six months when vigorous exercise programs were conducted.[7] Ingestion of Vitamin D and diphosphonates has had no beneficial effect.

One hypothesis is that microgravity stimulates bone resorption through altered bioelectric fields or altered tension and pressures on bone cells themselves.[8] On earth, muscular tensions caused by gravitation may cause bone crystals to produce bioelectrical fields, thus stimulating bone cells and affecting bone remodelling. Laboratory tests on centrifuged animals show that muscle atrophy and osteoporosis are inhibited. Artificial gravity on space stations would therefore help to ensure lower bone loss.

Further studies on neuroendocrine levels (e.g., PTH, calcitonin) of astronauts should be performed, as well as bone biopsies. The effects of estrogen loading on female astronauts may be an important study in the prevention of hypogravitational osteoporosis.

Fluid and electrolyte balance

Weightlessness removes gravity-induced hydrostatic pressure. Consequently, body fluids redistribute in a cephalad direction, and skin elasticity redistributes about 2 L of extracellular fluid into the circulatory system. This increase in thoracic blood volume is believed to initiate a Gauer-Henry reflex, wherein the stretch receptors in the left atrium inhibit the release of anti-diuretic hormone, resulting in spontaneous diuresis from the kidney, and reduction in plasma volume and electrolytes. In simulated bedrest studies, a 13% reduction in plasma volume was noted after four to five days. Although more difficult to measure in flight, increases in urinary electrolytes and decreases in ADH during space flights support this theory.[6] Mineral corticoid (9 alpha-fluorohydrocortisone) ingestion during bedrest studies was an effective countermeasure.[9] In contrast to men, women in the pre-ovulatory phase of their menstrual cycle showed no such decrease.[10]

Hematopoietic system

Along with plasma volume, red cell volume decreases. Current theory assumes that the cause is a suppression of new red cell production in the bone marrow. The decrease appears to stabilize at about 60 days in flight, and gradual recovery follows.[6] Changes occur in cell shape whereby a larger number become ellipsoidal and spherical; these changes reverse post flight. Microgravity is also an immunosuppressant, and the cause and significance of this observation need further study.

Neuromuscular system

Weightlessness "unloads" the musculoskeletal system. Postural tone is absent, and the body actually increases in length by about 5 cm. There is a decrease in body weight and mass; one-third of the weight loss derives from a decrease in lean body mass and fat.[6] Notable muscle changes are atrophy, an increase in circulating muscle enzymes, and a negative nitrogen balance. Atrophy and diminished strength occur, particularly in postural muscles. Studies on rhesus monkeys[8] indicate a breakdown of myofibrils and possible replacement by fibrous tissue. Electromyographic changes and altered deep-tendon reflexes have been noted. On the Soyuz T-5, 211-day Soviet mission, the astronauts became so weak that they had to be carried from the spacecraft. Wearing "Bungee" spacesuits, in which every body motion is resisted by a spring, was useful in reducing both atrophy and osteoporosis, but the suits were found to be cumbersome and had to be worn six to eight hours per day to achieve the desired effect. The effect of other flight-exercise programs is uncertain.

Cardiovascular system

Three major changes noted as a result of space flight are decreased orthostatic tolerance, altered cardiac electromechanics, and altered exercise capacity post flight. Echocardiographic studies on Skylab missions observed decreases in left ventricular volume without changes in contractile properties.[11] Studies conducted on Salyut 7 noted a small but reversible decrease in left ventricular muscle mass; this decrease was thought to be caused by loss of intercellular hydration.[12] Arrythmias noted during space flight may be the result of neuroendocrine and electrolyte imbalances induced by weightlessness.[6] Orthostatic intolerance during and after space flight is only partly the result of the volume losses. Replacement of these losses did not completely restore tolerance, and other factors include changes in venous compliance, and neurogenic and hormonal control mechanisms. To prevent "gray-out" during re-entry, ingestion of a litre of saline solution prior to re-entry has been helpful. Exercise capacity is severely reduced following space flight, but this reduction appears to be reversible within three weeks post flight. Exercise tolerance increased during spaceflight: astronauts were able to perform higher exercise intensities than they could in a one-gravity environment. This increase in ability is likely the result of the hemodynamic changes associated with microgravity.

Endocrine system

Because of multiple factors occurring simultaneously — zero gravity, motion sickness, dietary changes, psychological stresses of confined space travel, and chronic disruption of circadian rhythm — hormonal responses are difficult to interpret. These include alterations of anti-diuretic hormone, angiotensin, aldosterone, epinephrine, norepinephrine, and serum cortisol.

Parathyroid hormone levels[13] were higher during Skylab's space flights than pre-flight levels, possibly to counterbalance the negative calcium-balance effect of elevated serum cortisol. Thyroxine and thyroid-stimulating hormone levels were increased during space flight, likely contributing to the increased protein, carbohydrate, and fat metabolism. Changes in plasma insulin are inconclusive.

Female reproductive system

Information on the effect of weightlessness on the female reproductive system is scarce. Brock and Fortney[14] have noted reduced plasma volumes in the simulated bedrest studies in women. Plasma volume becomes normal in mid cycle during the preovulatory estrogen peak, likely as a result of the sodium-retaining effect of estrogen. In studying the effect of bedrest on the menstrual cycle, a luteal phase deficiency was noted in some patients. Further studies are needed on the effects of weightlessness on the hypothalamic-pituitary axis. It may be that alterations in the secretion of gonadotropins and in the levels, metabolism, and clearance of steroids, as well as the effect of cosmic irradiation on gonads and the pituitary in space flight, may result in alterations to ovulation in microgravity. Hence, amenorrhea, menometrorrhagia or hypermenorrhea may result. The effect of microgravity on normal hemostatic mechanisms is unknown.

A study by Wood and colleagues[15] considered whether cosmic radiation at levels that female astronauts would be exposed to in sun flares would lead to the development of endometriosis. In this study, 128 rhesus monkeys were subjected to proton irradiation and followed during their lifetime of about 13 years. Endometriosis in this mammal has a relatively low rate of occurrence in comparison to the rate in humans. An almost threefold increase in incidence that was statistically significant was found in study animals as compared to controls; in some cases endometriosis occurred as early as six years post irradiation. McLure and colleagues[16] suggest that irradiation may alter the immunological response of the host, promoting extrauterine location and proliferation of endometrial tissue. In space, where higher energy protons comprise a larger percentage of the cosmic radiation spectrum, secondary radiation by particle-collision interactions in human tissue will add to the radiation effect. Scott and colleagues[17] surgically induced endometriosis in monkeys by shifting uterine position to create intra-abdominal menstrual egress. Here, endometriosis developed as early as 75 days. This result is of some concern to the human female astronaut population, since the natural egress of menstrual fluid out through the vagina is, in the absence of gravitation, no greater, theoretically, than that through the fallopian tubes.

Conception and Gestation

An unnoticed (missed) pregnancy at the time of take-off for a six-month space-station mission or a possible normal ovulatory cycle while on the mission is a possibility. Assuming mixed crews, and even married couples on longer missions, what is known at present about the possibility of conception? If water immersion on earth is a realistic physiological simulation, then it can be assumed that coitus can be achieved with some degree of pleasure, much as it can be by a couple enjoying a swimming pool in other than conventional ways. The effect of microgravity on the male testes was studied by Philpert and colleagues[18] using male rats flown on space-shuttle mission SL-3. This experiment showed a 7.1% weight loss and reduction in spermatogonial cell population as compared to controls. These results correlate with previous experiments on dogs on a Cosmos 110 mission. It is not clear, however, whether the observed results were caused by stress or by exposure to microgravity. Many earlier studies by Hans Selye and others have shown that gonadal atrophy always occurred as a physiological response to non-specific stress, with recovery on stress removal. Another unknown factor is the effect of microgravity per se on sperm motility and directionality, or on transport of oocytes through the fallopian tubes.

Biological experiments in space on various cell cultures, including human lung-tissue cells, did not demonstrate any difference in mitotic index, migration rate, or duration of cell cycle.[19] The growth curve and cell ultrastructure were found to be unchanged. Similarly, a study of cultured human embryonic kidney cells[20] found no change in ability to differentiate into the four normal morphological types as a result of microgravity exposure. Studies of other biological objects exposed to microgravity for one to two months demonstrated no effect on basic development stages or the course of the majority of biological processes, though there was substantial concern about the effect of heavy nuclei cosmic radiation on the developing central nervous system.

The effect of microgravity on gestational development has been elegantly studied by Alperts and colleagues.[21] In this experiment, pregnant rat dams were flown on a Soviet flight in December 1983 for five days. The dams subsequently delivered normal offspring, but were, on average, 60 gm lighter in weight at the time of satellite recovery than were controls. Offspring of the flight group were similarly of lower mean body weight, but not significantly lower than offspring of controls subject to the same environmental conditions except for microgravity. Furthermore, the vestibular and olfactory functions, as well as visual, tactile, and auditory sensitivity, of flight offspring were normal, suggesting that mammalian ontogenesis is not vitally dependant on gravitational forces.

Earlier trauma research on automotive accidents, particularly the original studies on pregnant baboons subjected to rapid decelerations, help us to understand the implications of shuttle take-off and re-entry on pregnancy. Fetal survival in these cases was linked mainly to maternal survival.[22] Fetal trauma included cranial fractures and hemorrhage. Ranga and colleagues[23] noted a disruption of cellular integrity of the myocardium in the fetuses of sacrificed pregnant rats post re-entry.

Numerous animal studies using centrifuges have been conducted on physiological alterations to hypergravity exposure for up to a year or more. The results of these studies have been summarized by Serova and colleagues.[24] Certainly at 2 G, rats and mice, after a period of adaptation, have a normal life span, fertilization capacity, and will to copulate. Much of the data on short-term exposure shows the physiological price of a typical stress reaction, including growth delay, involution of lymph organs, and lymphopenia. This is the largest variable in terms of significance. The data can, in part, be extrapolated to microgravity. As with microgravity, short-term exposure of gestated rats to hypergravity resulted in similar decreased fetal mass, no decreases in calcium content of experimental fetuses relative to controls, but delayed skeletal development involving a 5%-20% reduction of ossification in virtually every bone. Maternal reaction was different. During gestation in microgravity, a greater than 50% decrease in calcium content was noted in maternal liver and kidney, whereas 2 G hypergravity did not produce this effect.

Overview

Current technology, particularly in transportation, has produced new environmental frontiers that have significant implications for the health and, in some cases, the survival of mother and fetus. The family physician should be aware of these risks, and the overlapping application of experimental findings between frontiers, where relevant. Developments by the turn of the century will direct significant attention to the issues surrounding cosmic radiation and microgravity. Some physical adaptive changes, such as hypogravitational osteoporosis, are partly irreversible and unless resolved may result in a situation where returning to the earth's gravitational environment is more physiologically hostile than remaining in space.

Conversely, the study of the fetus in a gestational sac in a 1-G earth environment, seen as a physiological model of microgravity, may help us to discover countermeasures to overcome hypogravitational osteoporosis and disuse muscular atrophy. These conditions may require sex-hormone therapy, particularly estrogens. Although, at present, women represent less than 3% of all astronauts, it may be that studies on the effect of estrogens in microgravity will make them more suitable astronauts than males. There may be some unique illnesses that are, in part, gravitationally induced, such as idiopathic scoliosis, that may eventually be treatable in space. ■

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